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the other of said strands comprises a compound [of claim 1] having chemical modifications that are resistant to single-stranded nucleases or increase affinity for the other strand of the substrate.

--94. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second

--94. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues having phosphodiester linkages and wherein said portions are base-paired with each other in said duplex.

95. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues that are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides includes a chemical modification that makes said oligonucleotide resistant to single-stranded nucleases.

96. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion that are base-paired with each other in said duplex; and

at least one of said first and said second oligonucleotides have a further portion that includes a chemical modification that increases the affinity of said oligonucleotide for the other oligonucleotide.

97. A double-stranded RNA comprising a duplex of a first oligonucleotide and a second oligonucleotide wherein said first and said second oligonucleotides each include a portion having at least four consecutive ribofuranosyl residues and where said portions are base paired with each other in said duplex; and

DOCKET NO.: ISIS-4313 Applicant submits that the claims as amended are in condition for allowance, and an early Office Action to that effect is earnestly solicited.

Respectfully submitted,

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